REMARKS

Prior to the present reply, claims 1, 56-80, and 85-89 were pending. Claims 85-89 are allowed. Claims 1 and 56-80 are rejected under 35 U.S.C. § 103(a) as being obvious over U.S. Patent No. 6,395,532 ("Jones"). This rejection is addressed below.

Claim amendments

Claim 73 has been amended to correct a minor typographical error. Claim 89 has been amended to recite pharmaceutically acceptable salts of Compound 22. Support for this change is found throughout the specification, for example, in original claim 1 and at page 31, lines 3-4. No new matter is added by the present amendment.

The invention

The present invention is directed to Lys-Gly and Gly-Lys dipeptides where the lysine amino acid side chain is modified at its ε-amino group by addition of $-CO-R_x$, where R_x is a hydrophobic group. The invention also features methods of using these peptides to treat arrhythmia.

Rejection under 35 U.S.C. § 103(a)

Claims 1 and 56-80 are rejected as being obvious over the teachings of Jones. In making this rejection, the Office asserts that Jones teaches Gly-Lys peptides bearing small or large hydrophobic side chains. Based on these teachings, the Office concludes that it

would be obvious to one of skill in the art to make Gly-Lys peptides having any type of side chain modification, asserting that Jones teaches that small and large hydrophobic side chain modifications may be carried out on Gly-Lys[1] dipeptides. Applicants respectfully disagree with the Office's interpretation of Jones and submit that the present claims are not prima facie obvious over Jones, as asserted by the Office.

Contrary to the Office's position, Jones does not teach side chain modifications either to lysine or to dipeptides. Rather, the section of Jones cited by the Office describes a coupling reaction between Z-L-Lys-OBn and Gly-NH_2, which produces the compound, Z-L-Lys-Gly-NH_2. As explained in Figure 5 of Jones, none of these compounds contains an amino acid having a modified side chain ("R" group). The "Z" group refers to a modification of the primary amino group on the amino acid, and the "OBn" group refers to a modification of the carboxyl moiety of the amino acid. Z-L-Lys-OBn has an amino acid side chain ("R") of $(CH_2)_4NH_2$, which represents an unmodified lysine side chain. Jones therefore does not teach lysine having a modified side chain. Likewise, Jones does not teach dipeptides having amino acids with modified side chains.

Jones also does not suggest a modified a lysine side chain, as asserted by the Office. The Office bases its rejection upon the following passage:

> Acyl donors Z-L-Phe-OBn, Z-L-Ala-OBn, Z-L-Glu-OMe, and Z-L-Lys-SBn (1-4) and acyl acceptors Gly-NH_2 and L-Ala-NH_2 (5, 6) were used for the coupling reaction as shown in FIG. **5**. The acyl donors Z-L-Phe-OBn, Z-L-Ala-OBn, Z-L-Glu-OMe, and Z-L-Lys-SBn (1-4) provided representative examples of large and small hydrophobic, negatively charged

[1]Jones does not teach Gly-Lys peptides. Rather, Jones teaches a Lys-Gly compound. Applicants therefore address the § 103(a) rejection in view of the Lys-Gly compound described in Jones.

> and positively charged P_1 side chains, respectively and allowed a broad evaluation of the affinity of the S_1 pocket of these enzymes for various amino acids.

Jones, column 16, lines 15-23. In its rejection, the Office asserts that the "large and small hydrophobic...side chains" referred to in this passage describe or suggest a lysine side chain modification. This is incorrect. Rather, Jones is characterizing the phenylalanine side chain of Z-L-Phe-OBn as a representative example of a "large" hydrophobic side chain and the alanine side chain of Z-L-Ala-OBn as a representative example of a "small" hydrophobic side chain. As such, Jones is not suggesting a modified lysine amino acid side chain at all.

Further, Jones does not teach or suggest a lysine side chain modified in the manner presently claimed. Claim 1 requires that the dipeptide contain a side chain: $(CH_2)_4$–NH–C(O)–R_x, where R_x is a hydrophobic group. Because unmodified lysine has a $(CH_2)_4$–NH_2 side chain, the side chain recited in claim 1 can also be described as a lysine side chain modified by addition of a –C(O)–R_x group at its ε-amino group. There is no teaching in Jones of a lysine having a –C(O)–R_x modification at its ε-amino group, and no suggestion in Jones to make such a modification.

Jones thus fails to teach or suggest any dipeptide having a modified side chain or a modified lysine side chain. Jones further fails to teach or suggest the particular modified lysine side chains recited in the present claims. Jones therefore cannot form the basis for rejecting claim 1 or its dependent claims as prima facie obvious. Withdrawal of the rejection under § 103(a) is therefore respectfully requested.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested. Enclosed is a Petition to extend the period for replying to the Office action for three (3) months, to and including July 27, 2009.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: July 14, 2009.

Kristina Bieker-Brady, Ph.D.
Reg. No. 39,109

Clark & Elbing LLP
101 Federal Street
Boston, MA 02110
Telephone: 617-428-0200
Facsimile: 617-428-7045